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Effects of selective and non-selective beta-adrenergic blockade on coronary dynamics in man assessed by rapid atrial pacing

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SUMMARY The effects on coronary dynamics of propranolol and atenolol were studied in 12 patients undergoing cardiac catheterisation for suspected coronary artery disease. Myocardial blood flow was measured using the coronary sinus continuous thermodilution technique. Data were obtained immediately after drug administration and during rapid atrial pacing. The immediate effects were similar for both drugs. A significant reduction in heart rate was accompanied by a small reduction in myocardial oxygen consumption. Changes in coronary sinus flow induced by rapid pacing were closely related to changes in tension-time index. This relation was not modified by propranolol or atenolol. Neither propranolol nor atenolol therefore has significant coronary vasoconstrictor properties. Cardioselectivity appears to be unimportant with respect to beta-adrenergic blockade and the coronary circulation.

The presence of alpha and beta-adrenergic receptors in the coronary vasculature of the dog has been shown (Parratt, 1965; Klocke *et al.*, 1965; Gaal *et al.*, 1966). Furthermore, there is evidence that selective beta-adrenergic blockade of the dog heart spares the beta-adrenergic receptors of the coronary vessels (Ross and Jorgensen, 1968; Bussmann *et al.*, 1970) suggesting that, like peripheral arterial systems, the coronary vasculature possesses so-called $beta_2$-adrenergic receptors. As a vasoconstrictive effect of non-selective beta-adrenergic blockade has been shown in animals (Parratt and Grayson, 1966) and in man (Wolfson *et al.*, 1966; Wolfson and Gorlin, 1969), presumably because of unopposed alpha-adrenergic vasoconstrictor activity, it appears that the use of a selective beta 1-blocking agent would be more appropriate in the treatment of angina pectoris.

Atenolol ('Tenormin')—4(2-hydroxy-3-isopropylaminopropoxy-phenylacetamide) has been shown to possess a significant degree of cardio-selectivity in animals (Barrett *et al.*, 1973) and in man (Marlin *et al.*, 1975). This drug was, therefore, compared with propranolol, a non-selective beta-adrenergic blocking drug with similar potency.

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Patients and methods

Twelve patients undergoing cardiac catheterisation for suspected coronary artery disease were studied. The 11 men and 1 woman, from whom informed consent was obtained, received 10 mg diazepam as premedication. All other medication was discontinued 48 hours before the study. There was no evidence of cardiac failure, obstructive airways disease, bradycardia, renal or hepatic failure, or cardiac conduction disturbance.

After left ventriculography and coronary arteriography (Seldinger technique from the femoral artery) a No. 5 Desilet-Hoffman cannula was placed in the femoral artery for arterial pressure monitoring and blood sampling. A Ganz thermodilution coronary sinus catheter with pacing electrodes was advanced to the coronary sinus via a left antecubital vein. Myocardial blood flow was determined by the method described by Ganz (Ganz *et al.*, 1971). These authors showed a good correlation between this and other standard methods. Coronary sinus flow is determined by a continuous thermodilution technique. The coronary sinus drains nearly all of the left ventricular myocardium (Hood, 1968) and coronary sinus flow may, therefore, be assumed to represent mainly left ventricular myocardial blood flow. To make this determination,

an injectate (5% dextrose) is delivered through an orifice near the tip of the catheter by a constant rate infusion pump. The temperature of the injectate is determined by a thermistor at the orifice, while that of the mixture of blood and injectate is determined by a proximally situated thermistor. Coronary sinus flow is calculated by a heat exchange formula described below. In an attempt to include the contribution to coronary sinus flow by the posterior interventricular vein which joins the coronary sinus near its orifice, close approximation of the proximal thermistor marker to the coronary sinus orifice was ensured by injection of contrast medium, before each determination. Blood samples were obtained through this catheter. Atropine 0·6 mg intravenously was administered to prevent possible vagal interactions (Glick and Braunwald, 1965). Arterial pressure was measured using a Bell and Howell transducer. Leads II and V5 of the electrocardiogram were recorded. Recording was by Elema Mingograf 82.

Blood oxygen contents were derived from oxygen saturations measured spectrophotometrically (IL CO oximeter). This method was first calibrated against the fuel-cell technique (Lex-O_2-Con) which has been found to give results in close agreement with those obtained using the manometric technique of Van Slyke (Valeri *et al.*, 1972; Adams and Cole, 1975).

Rapid atrial pacing has been shown to produce increases in coronary sinus flow in patients with and without coronary artery disease (MacLeod *et al.*, 1973). Incremental increases in heart rate by pacing produce an identical linear response in normal subjects and in those with coronary artery disease to the point of development of angina (Yoshida *et al.*, 1971). Rapid atrial pacing was, therefore, used in this study as a technique for augmenting possible effects on the coronary vasculature of propranolol and atenolol, in patients with and without coronary artery disease.

After the elapse of at least 30 minutes from the time of left ventricular angiography, measurements of heart rate, systemic arterial pressure, and coronary sinus flow were made. Simultaneous arterial and coronary sinus blood samples were obtained for oxygen content estimation. The heart rate was then increased by pacing by increments of 10 beats a minute until the onset of angina (when the pacing rate was reduced until this symptom was alleviated), atrioventricular block, or ST-T changes on the electrocardiogram developed, or 150 beats/minute (160 in one patient) was achieved. Measurements were then repeated. (In some patients additional measurements were made at lower pacing rates.) Pacing was then terminated. At 10 minutes control measurements were repeated after which 0·1 mg/kg propranolol or atenolol, randomly selected, was administered intravenously. Measurements were repeated at 10 minutes in sinus rhythm and with the heart rate paced at the rate immediately preceding administration of the drug. Further measurements were then made during rapid atrial pacing as before.

Mean left ventricular systolic pressure and systolic ejection period were derived from the arterial pressure trace (Mueller *et al.*, 1974).

CALCULATIONS

Tension-time index (mmHg − s/min) = mean left ventricular systolic pressure[1] × systolic ejection period[1] × heart rate

Coronary sinus flow ml/min

$$= \frac{T_M - T_I}{T_B - T_M} \times K \times Q_I$$

where T_M = temperature of mixture of blood and injectate, °C; T_I = temperature of injectate, °C; T_B = temperature of blood, °C; K = a constant relating specific heat and density of blood and injectate (1·08); and Q_I = rate of infusion of injectate, ml/min (36 ml/min).

Myocardial oxygen consumption, ml/min = coronary sinus flow × coronary arteriovenous oxygen content (AV O_2) difference.

DATA ANALYSIS

The data analysis was performed in the following way.

Comparisons between (a) before and after drug with heart rate free and with the heart paced to control rate after beta-blockade, (b) before and after drug during rapid atrial pacing.

(Statistical analysis by paired t test.)

The relation between tension-time index and coronary sinus flow was examined by regression analysis.

Results

INITIAL HAEMODYNAMIC AND CINEANGIOGRAPHIC DATA

The left ventricular end-diastolic pressure and ejection fraction were normal in all patients. In 10 patients there was significant coronary artery disease while in 2 patients the coronary arteries were normal (Table 1).

[1]Systolic ejection period was measured from the upstroke of the femoral artery pressure record to the dicrotic notch. The mean femoral arterial pressure during this period was taken as a measure of mean left ventricular systolic pressure.

Table 1 *Coronary arteriographic data*

Propranolol group				*Atenolol group*			
Case No.	*Age (y)*	*Sex*	*Coronary arteriogram*	*Case No.*	*Age (y)*	*Sex*	*Coronary arteriogram*
1	51	M	100% LAD, >75% RCA	7	49	F	Normal
2	48	M	>75% LAD, >50% CX, >70% RCA	8	46	M	>75% LAD and CX
3	50	M	>50% left main, >50% LAD and CX, >75% RCA	9	27	M	Normal
4	45	M	>50% LAD	10	43	M	>75% LAD
5	54	M	>90% LAD, >75% CX, >75% RCA	11	51	M	>75% LAD and CX
6	51	M	100% LAD, >75% RCA	12	44	M	>75% LAD

Percentage figures refer to degree of coronary arterial stenoses.
LAD, left anterior descending branch; CX, circumflex branch; RCA, right coronary artery.

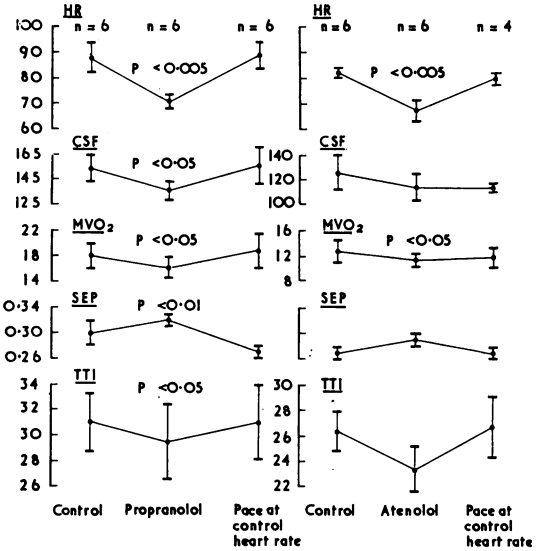

Fig. 1 *Immediate effects of propranolol and atenolol. HR, heart rate, beats/minute; CSF, coronary sinus flow, ml/minute; MVO_2, myocardial oxygen consumption, ml/minute; SEP, systolic ejection period, seconds; TTI, tension-time index, mmHg s/min ($\times 10^{-2}$).*

IMMEDIATE EFFECTS OF DRUGS

Propranolol

Propranolol produced a significant fall in mean heart rate (20%). This was associated with significant falls in mean coronary sinus flow (12%), myocardial oxygen consumption (11%), and tension-time index (5%). There was a significant increase (10%) in mean systolic ejection period (Fig. 1). Mean coronary AV O_2 difference and mean left ventricular systolic pressure remained unchanged. Individual data are presented in Table 2.

Atenolol

Atenolol produced a similar pattern of changes with falls in mean heart rate (18%), coronary sinus flow (11%), myocardial oxygen consumption (13%), and tension-time index (12%). Mean systolic ejection period increased by 7 per cent. The falls in coronary sinus flow and tension time index just failed to reach statistical significance ($P < 0{\cdot}10$) (Fig. 1). Like propranolol, atenolol produced no significant change in mean coronary AV O_2 difference or mean left ventricular systolic pressure. Data for individual patients are presented in Table 3.

Table 2 *Effects of propranolol on coronary haemodynamics*

Control							*10 minutes after propranolol*						
Case No.	*HR*	*CSF*	*AV O_2 diff.*	*MVO_2*	*SEP*	*LVSP*	*TTI*	*HR*	*CSF*	*AV O_2 diff.*	*MVO_2*	*SEP*	*LVSP*	*TTI*
1	94	170	12·1	20·6	0·28	102	2691	72	157	11·8	18·5	0·32	109	2519
2	90	118	11·0	13·0	0·30	122	3288	77	117	11·3	13·2	0·32	123	3033
3	82	136	15·0	20·4	0·30	154	3799	65	130	15·3	20·0	0·34	178	3924
4	110	194	12·5	24·2	0·22	113	2724	75	133	13·3	17·7	0·30	107	2415
5	65	176	10·1	17·8	0·34	111	2455	58	163	10·1	16·5	0·34	105	2068
6	90	128	9·3	11·9	0·28	147	3717	75	112	9·2	10·3	0·32	154	3696
Mean	88	154	11·7	18·0	1·29	125	3112	70	135	11·8	16·0	0·32	129	2942
SEM	6·0	12·4	0·83	1·9	0·02	8·6	233	3·0	8·5	0·9	1·5	0·01	12·3	303
P								<0·005	<0·05	NS	<0·05	<0·01	NS	<0·05

HR, heart rate (beats/min); MVO_2, myocardial oxygen consumption (ml/min); TTI, tension-time index (mmHg-s/min); CSF, coronary sinus flow (ml/min); SEP, systolic ejection period (s); SEM, standard error of mean; AV O_2 diff., coronary arteriovenous oxygen content difference (ml/100 ml); LVSP, mean left ventricular systolic pressure (mmHg); P, significance.

Table 3 *Effects of atenolol on coronary haemodynamics*

Control								*10 minutes after atenolol*						
Case No.	*HR*	*CSF*	*AV O_2 diff.*	*MVO_2*	*SEP*	*LVSP*	*TTI*	*HR*	*CSF*	*AV O_2 diff.*	*MVO_2*	*SEP*	*LVSP*	*TTI*
7	84	126	10·0	12·6	0·30	129	3242	68	120	10·2	12·2	0·32	135	2941
8	78	121	11·5	13·9	0·28	125	2625	56	84	11·2	9·0	0·28	105	1646
9	80	192	9·7	18·6	0·26	117	2444	70	156	10·0	15·6	0·28	115	2249
10	85	127	10·3	13·1	0·26	130	2873	60	116	11·0	12·8	0·28	142	2390
11	75	71	10·0	7·1	0·30	91	2055	64	82	9·8	8·0	0·32	107	2193
12	90	126	11·0	13·9	0·24	120	2592	85	120	9·6	11·5	0·25	120	2559
Mean	82	127	10·4	13·2	0·27	119	2638	67	113	10·2	11·5	0·29	118	2330
SEM	2·2	14·3	0·3	1·8	0·001	5·9	163	4·1	11·2	0·22	1·1	0·011	6·1	175
P								<0·0025	NS	NS	<0·05	<0·0025	NS	NS

For key to abbreviations see Table 2.

EFFECTS OF RESTORING HEART RATE

When the heart rate was artificially restored to that immediately preceding drug administration, systolic ejection period and tension time index returned to control levels. Similar effects on coronary sinus flow and myocardial oxygen consumption were observed (Fig. 1 and Tables 4 and 5).

CORONARY HAEMODYNAMICS DURING RAPID ATRIAL PACING

Coronary sinus flow increased in all patients during rapid atrial pacing. Atrioventricular block developed in some patients after drug administration, preventing the achievement of identical heart rates. However, where it was possible to compare data for identical heart rates no significant changes were observed after either drug except for a fall in mean coronary sinus flow after propranolol (Tables 6 and 7). Significant falls occurred in 3 patients. There was a corresponding fall in mean myocardial oxygen consumption but this did not reach statistical significance. Individual responses to rapid atrial pacing before and after propranolol and atenolol are seen in Fig. 2 and 3.

Table 4 *Effects of propranolol on coronary haemodynamics*

Control								*Pace to control heart rate*						
Case No.	*HR*	*CSF*	*AV O_2 diff.*	*MVO_2*	*SEP*	*LVSP*	*TTI*	*HR*	*CSF*	*AV O_2 diff.*	*MVO_2*	*SEP*	*LVSP*	*TTI*
1	94	170	12·1	20·6	0·28	102	2691	94	159	12·0	19·1	0·26	107	2621
2	90	118	11·0	13·0	0·30	122	3288	90	123	11·0	13·5	0·28	127	3213
3	82	136	15·0	20·4	0·30	154	3799	82	172	15·1	26·0	0·28	181	4167
4	110	194	12·5	24·2	0·22	113	2724	110	213	12·8	27·3	0·24	110	2904
5	65	176	10·1	17·8	0·34	111	2455	65	163	10·2	16·6	0·30	107	2093
6	90	128	9·3	11·9	0·28	147	3717	90	109	10·3	11·2	0·28	143	3600
Mean	88	154	11·7	18·0	1·29	125	3112	88	156	11·9	18·9	0·27	129	3100
SEM	6·0	12·4	0·83	1·9	0·02	8·6	233	6·6	15·1	0·76	2·7	0·01	11·9	299
P								NS	NS	NS	NS	NS	NS	NS

For key to abbreviations see Table 2.

Table 5 *Effects of atenolol on coronary haemodynamics*

Control								*Pace to control heart rate*						
Case No.	*HR*	*CSF*	*AV O_2 diff.*	*MVO_2*	*SEP*	*LVSP*	*TTI*	*HR*	*CSF*	*AV O_2 diff.*	*MVO_2*	*SEP*	*LVSP*	*TTI*
7	84	126	10·0	12·6	0·30	129	3242	84	103	10·2	10·5	0·30	125	3164
8	78	121	11·5	13·9	0·28	125	2625	78	124	11·2	13·9	0·26	116	2347
9	80	192	9·7	18·6	0·26	117	2444	—	—	—	—	—	—	—
10	85	127	10·3	13·1	0·26	130	2873	85	134	10·9	14·6	0·26	137	3016
11	75	71	10·0	7·1	0·30	91	2055	75	92	9·8	9·0	0·28	105	2205
12	90	126	11·0	13·9	0·24	120	2592	—	—	—	—	—	—	—
Mean	82	127	10·4	13·2	0·27	119	2638	80	113	10·5	12·0	0·27	121	2683
SEM	2·2	14·3	0·3	1·8	0·001	5·9	163	2·4	2·4	0·32	1·3	0·01	6·8	2·39
P									NS	NS	NS	NS	NS	NS

For key to abbreviations see Table 2.

Table 6 *Effects of propranolol on coronary haemodynamics during rapid atrial pacing*

Rapid atrial pacing—control								*Rapid atrial pacing after propranolol*						
Case No.	*HR*	*CSF*	*AV O_2 diff.*	*MVO_2*	*SEP*	*LVSP*	*TTI*	*HR*	*CSF*	*AV O_2 diff.*	*MVO_2*	SEP	*LVSP*	*TTI*
1	160	278	13·7	38·2	0·20	144	4619	150	299	13·3	39·8	0·20	166	4990
2*	140	333	12·4	41·3	0·22	103	3168	140	275	11·5	31·6	0·18	107	2700
3*	150	208	10·9	22·7	0·22	121	3998	150	210	11·6	24·4	0·22	127	4196
4*	140	295	12·9	38·0	0·20	112	3136	140	232	11·9	27·6	0·20	106	2977
5*	120	211	10·1	21·3	0·24	110	3159	120	208	10·9	22·7	0·24	111	3184
6*	150	185	9·4	17·4	0·20	150	4510	150	166	10·1	16·7	0·20	134	4020
Mean	140	246	11·1	28·1	0·22	119	3594	140	218	11·2	24·6	0·21	117	3415
SEM	5·5	28·6	0·7	4·8	0·01	8·2	281	5·5	17·8	0·3	2·5	0·01	5·7	294
P									<0·05	NS	NS	NS	NS	NS

For key to abbreviations see Table 2.
*Means, SEM, and significance given for these patients only.

Table 7 *Effects of atenolol on coronary haemodynamics during rapid atrial pacing*

Rapid atrial pacing—control								*Rapid atrial pacing after atenolol*						
Case No.	*HR*	*CSF*	*AV O_2 diff.*	*MVO_2*	*SEP*	*LVSP*	*TTI*	*HR*	*CSF*	*AV O_2 diff.*	*MVO_2*	*SEP*	*LVSP*	*TTI*
7	150	180	10·0	18·0	0·22	115	3781	130	180	9·9	17·8	0·22	117	3346
8	140	150	10·4	15·6	0·22	118	3641	125	164	9·8	16·1	0·24	109	3257
9*	110	154	11·8	18·2	0·24	118	3115	110	143	11·9	17·0	0·22	111	2676
10*	110	194	10·0	19·4	0·22	111	2698	110	230	10·1	23·2	0·22	116	2814
11*	140	162	10·0	16·3	0·20	143	4013	140	155	10·7	16·6	0·22	118	3643
12*	150	195	9·8	19·1	0·20	109	3270	150	185	10·1	18·7	0·20	105	3140
Mean	127	176	10·4	18·2	0·22	120	3274	127	178	10·8	19·0	0·22	112	3068
SEM	10·3	10·7	0·5	0·7	0·01	7·8	274	10·3	19·4	0·5	1·5	0·01	2·9	215
P									NS	NS	NS	NS	NS	NS

For key to abbreviations see Table 2.
*Means, SEM, and significance given for these patients only.

RELATION BETWEEN CORONARY SINUS FLOW AND TENSION-TIME INDEX

When all values for coronary sinus flow were plotted against tension-time index for individual patients a highly significant linear correlation was obtained (Fig. 4 and 5). Thus, values obtained before and after either drug fell on the same regression line.

Discussion

The relatively few published reports concerning the effects of propranolol on the coronary vasculature in man present a confusing picture. While a reduction in myocardial blood flow associated with widening of the coronary AV O_2 difference has been reported (Wolfson *et al.*, 1966; Wolfson and Gorlin, 1969) suggesting a vasoconstrictor effect, others have shown reductions in myocardial blood flow with narrowing of the coronary AV O_2 difference (Mueller *et al.*, 1974). Significant falls in myocardial blood flow after propranolol administration were observed by Reale *et al.* (1970) in patients with normal coronary arteries while Lewis and Brink (1968) found no change in mean myocardial blood flow or AV O_2 difference after propranolol in patients with coronary artery disease.

In the present study propranolol produced relatively small falls in coronary sinus flow without significantly affecting the AV O_2 difference. Consequently there was a comparable fall in myocardial oxygen consumption. Similar changes were observed with atenolol. As heart rate, a major determinant of myocardial oxygen consumption (Sarnoff *et al.*, 1958), fell significantly a greater fall in the latter may have been expected. However, it is seen that there is a simultaneous increase in the duration of systole, as previously observed (Sowton and Hamer, 1966) after propranolol. This tends to increase myocardial oxygen consumption (Sarnoff *et al.*, 1958) and thus offset the effect of heart rate reduction. Further, propranolol has been shown to increase left ventricular end-diastolic volume (Chamberlain, 1966; Helfant *et al.*, 1971) and thus myocardial wall tension; a change known to increase myocardial oxygen consumption (Taylor *et al.*, 1967; Graham *et al.*, 1968). In contrast, the reduction by propranolol of myocardial contractility (Wolfson *et al.*, 1966; Lewis and Brink, 1968) would have

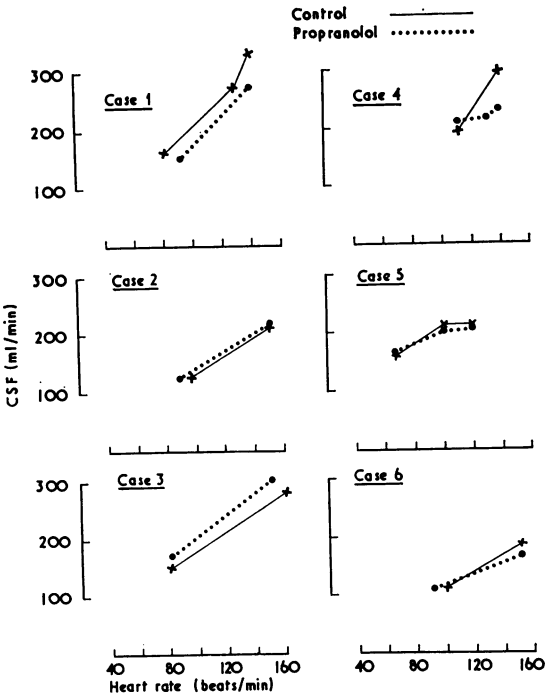

Fig. 2 *Effects of rapid atrial pacing before and after propranolol for individual patients. CSF, coronary sinus flow, ml/minute.*

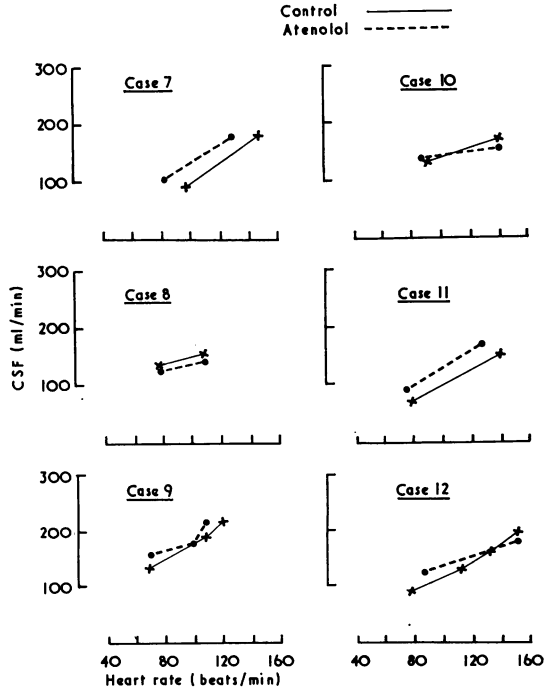

Fig. 3 *Rapid atrial pacing before and after atenolo for individual patients. CSF, coronary sinus flow, m/minute.*

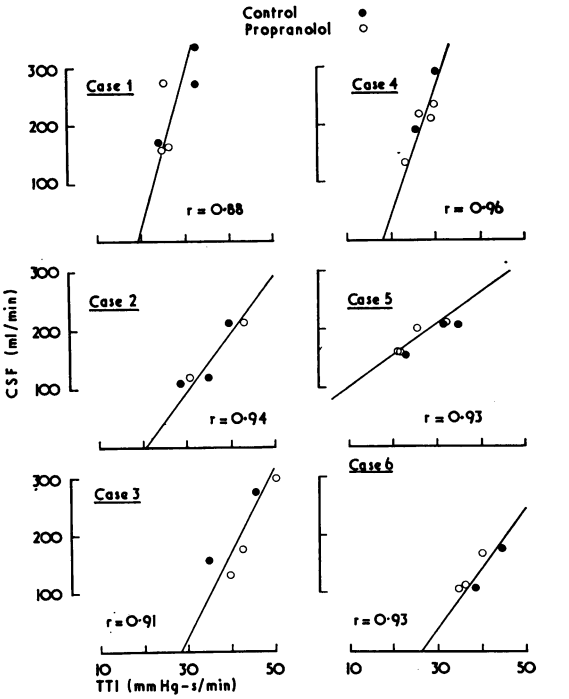

Fig. 4 *Relation between tension-time index (TTI—$\times 10^{-2}$) and coronary sinus flow (CSF) for individual patients (propranolol group).*

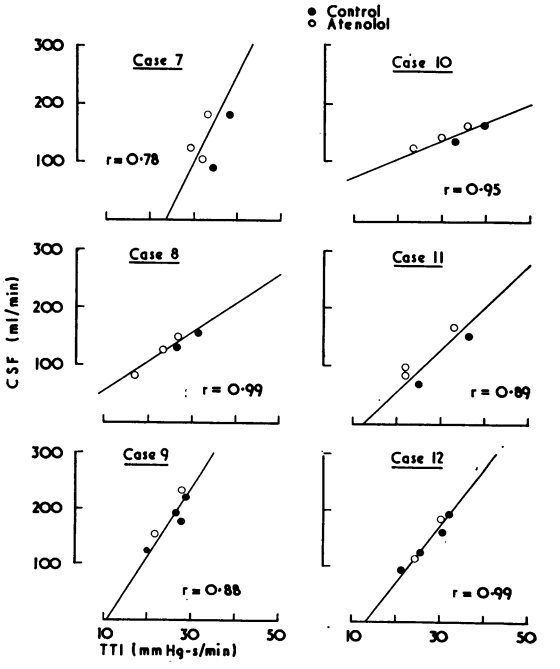

Fig. 5 *Relation between tension-time index (TTI—$\times 10^{-2}$) and coronary sinus flow (CSF) for individual patients (atenolol group).*

the opposite effect (Sonnenblick *et al.*, 1965; Graham *et al.*, 1968).

It is clear, therefore, that the net effect of propranolol on myocardial oxygen consumption depends upon the relative prevailing influences of these separate variables. In this study the restoration of heart rate after beta-adrenergic blockade, with the consequent return to control levels of the systolic ejection period, cancelled the observed changes in myocardial oxygen consumption. This suggests that these variables are the major determinants of the net effect of these agents on myocardial oxygen consumption at rest. Since depression of contractility would be unaffected by the restoration of heart rate, it is unlikely that beta-adrenergic blockade produced this effect to an important degree, since a persistent reduction of myocardial oxygen consumption would then be expected.

The increase in coronary sinus flow produced by rapid atrial pacing is probably in response to increased myocardial oxygen demand as a result of augmentation of the rate of left ventricular force development (Sonnenblick *et al.*, 1966). If propranolol causes coronary vasoconstriction, the appearance of a disparity between myocardial oxygen demand and supply would be expected. This would show as a reduction in myocardial blood flow or a widening of the coronary AV O_2 difference, or a combination of both. However, a reduction in myocardial blood flow (myocardial oxygen supply) may result from a reduction in myocardial oxygen demand, since myocardial blood flow is controlled by an autoregulatory mechanism depending on local metabolites which influence coronary vascular tone (Berne, 1964). Therefore, a reduction in myocardial blood flow after the administration of a given drug cannot *per se* be said to represent an inappropriate or non-physiological, coronary vasoconstrictive effect of that drug. In this study, it is seen that after propranolol, but not atenolol, there was a significant reduction in mean coronary sinus flow during rapid pacing. There was an accompanying fall not reaching statistical significance in mean myocardial oxygen consumption. It may be argued that this represents a direct, that is non-physiological vasoconstrictive effect of propranolol. To analyse these changes further, it is pertinent to examine the relation between myocardial oxygen demand and supply. The former has been shown to correlate closely with the tension-time index (Sarnoff *et al.*, 1958) while the latter may be represented by coronary sinus flow as previously discussed. As can be seen in Fig. 4 and 5, there is a high degree of correlation between these two variables for individual patients independent of the actions of either propranolol or atenolol. Changes in coronary sinus flow, therefore, result solely from changes in myocardial oxygen demand, not from any direct influence of the drugs on coronary vascular tone.

The close relation between coronary sinus flow and tension-time index shown in this study suggests that the measurement of coronary sinus flow is an accurate technique for deducing changes in myocardial blood flow reproducible over a wide range of flows.

CLINICAL IMPLICATIONS

Beta-adrenergic blocking drugs are used specifically in the resting patient with coronary artery disease: for example in certain patients with acute myocardial infarction, where a reduction in myocardial oxygen consumption is desired. The results of this study however suggest that the degree of such a reduction achieved by beta-adrenergic blockade may be modest. Thus, though beta-adrenergic blockade may for example effectively reduce heart rate in such patients a parallel reduction in myocardial oxygen consumption cannot necessarily be expected. It is probable that the more important role of such therapy is that of the prevention of tachycardia induced, for example, by emotional stress, since a rise in heart rate may result in significant augmentation of myocardial oxygen consumption.

Atenolol appears to possess similar coronary haemodynamic properties to those of propranolol. Its importance with respect to its cardioselectivity may, therefore, be confined to use in those patients with coronary artery disease who have coexisting obstructive airways disease. Conversely, its cardioselectivity with respect to the coronary and peripheral vasculature may become important in the exercising patient with angina pectoris when circulating catecholamine activity is augmented, since possible coronary or peripheral vasoconstrictive properties of propranolol may then become manifest. Such a possibility requires further investigation.

The relatively minor changes in coronary dynamics observed after beta-adrenergic blockade in this study suggest that a direct effect of these agents on the myocardium or coronary vasculature is unlikely to have therapeutic relevance in the ambulant patient with angina pectoris. It is probable that their importance in this respect lies solely in their ability to reduce the degree of exertional tachycardia and hence myocardial oxygen demand.

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